

**REMARKS**

In the Office Action mailed 01 July 2003, by Examiner Chakrabarti, in Art Unit 1634, Claims 1-4, 6, 9, 11-47 are pending and all stand rejected. By the present Response and Amendment, Applicant has amended Claims 1 and 41-43. Applicant thanks the Examiner for his kind suggestions and comments. In light thereof, Applicant submits that the present amendment clarifies the invention and does not require additional searching by the Examiner. Reconsideration of the Patent Office's rejections is respectfully requested in view of the amendments to the Claims and the accompanying remarks.

**I. AMENDMENT OF THE CLAIMS**

Claims 1 and 41-43 have been amended to clarify the term "four required types of nucleotides for continuous extension during primer extension reactions" by replacing it with --A, T, G, or C non-terminator nucleotides--. Claims 1 and 41 are further amended to clarify that a nucleotide which is not omitted is labeled with a detectable marker. Basis for this amendment is found in the application as originally filed, for example on page 10, first full paragraph. Applicant respectfully submits that the claims are directed to a method using a non-terminator nucleotide reaction mixture that contains an incomplete set of nucleotides such that a full length transcription product of a template cannot be formed. A full length transcript of the template cannot be formed because one of A, T, G, or C nucleotides is not present in the non-terminator nucleotide reaction mixture. Claim 1 is further amended to clarify that at least one non-terminator nucleotide of the non-terminator nucleotide mixture is labeled with a detectable marker. Thus, the reaction mixtures of the claimed subject matter have two different purine nucleotides and one pyrimidine nucleotide, or two different pyrimidine nucleotides and one purine nucleotide.

**II. REJECTION OF CLAIMS 1-4, 6, 9, and 11-15, 18, 20-24, 42, 45, and 47 UNDER 35 U.S.C. § 102(a)**

Claims 1-4, 6, 9, and 11-15, 18, 20-24, 42, 45, and 47 are rejected anticipated by U.S. Pat. No. 5,521,296 to Okada et al. under 35 U.S.C. § 102(a) because Okada et al. allegedly discloses

each and every element of the claimed subject matter. Applicant respectfully traverses this rejection because Okada et al. fails to disclose, among other things, a non-terminator nucleotide reaction mixture wherein at least one of A, T, G, or C nucleotides is omitted.

The Office Action cites column 12, lines 35-46, as disclosing a non-terminator nucleotide reaction mixture wherein at least one of A, T, G, or C nucleotides is omitted. Applicant respectfully disagrees. Okada et al. teaches a reaction mixture having, among other things, 0.1 mM dATP, dTTP, dGTP, and 5  $\mu$ l of  $\alpha$ -<sup>32</sup>P-dCTP. Thus, the reaction mixture of Okada et al. has two purines (dATP and dGTP) and two pyrimidines (dTTP and dCTP). All of the four types of nucleotides, A, T, G, and C, are present in the reaction mixture of Okada et al. Therefore, Applicant submits that Okada et al. does not anticipate the claims 1 or 42 or claims dependent on claims 1 or 42.

Applicant notes that dependent claim 6 identifies exemplary combinations of non-terminator nucleotides of the non-terminator nucleotide reaction mixture. As demonstrated in the nucleotide groups of claim 6, one of A, T, G, or C is omitted from the nucleotide reaction mixture.

### **III. REJECTION OF CLAIM 43 UNDER 35 U.S.C. § 102(b)**

Claim 43 is rejected as anticipated by Fahey et al. (1997) Nucleic Acid Research 25:3102-3109 because Fahey et al. allegedly discloses each and every element of claim 43. Applicant respectfully traverses this rejection because Fahey et al. fails to disclose, among other things, a non-terminator nucleotide reaction mixture wherein at least one of A, T, G, or C nucleotides is omitted.

The Office Action cites the Abstract and Materials and Methods Section of Fahey et al. as disclosing the claimed method. Applicant respectfully submits that the cited passages of Fahey et al. do not disclose the claimed subject matter. The Abstract of Fahey et al. expressly provides that primer extension products of different lengths are formed to investigate mutations in mitochondrial DNA. Claim 43 recites the formation of isometric primer extension products. Isometric primer extension products are all of the same length (see page 5 of the specification). Accordingly, Fahey et al. cannot anticipate claim 43.

In addition, Table 2 of Fahey et al. discloses the use of terminator nucleotides in the primer extension reaction mixture. The terminator nucleotides are dideoxy nucleotides. Claim 43 expressly recites the use of non-terminator nucleotides. Fahey et al. does not disclose forming isometric primer extension products by omitting one of A, T, G, or C from a non-terminator nucleotide reaction mixture. In fact, Fahey et al. discloses adding terminator nucleotides to the reaction mixture. Thus, Fahey et al. cannot anticipate claim 43.

#### IV. REJECTION OF CLAIM 41 UNDER 35 U.S.C. § 102(e)

Claim 41 is rejected as anticipated under 35 U.S.C. § 102(e) over U.S. Patent No. 6,221,592 to Schwartz et al. because Schwartz et al. allegedly discloses all of the claim elements. Applicant respectfully traverses this rejection because Schwartz et al. fails to disclose among other things, forming isometric primer extension products incorporating at least one fluorescently labeled nucleotide by omitting at least one of A, T, G, or C nucleotides.

The Office Action points to the Abstract and Figure 3 of Schwartz et al. as disclosing all of the elements of claim 41. Applicant points out that the Abstract specifically references using dideoxy nucleotides. Dideoxy nucleotides are terminator nucleotides (see pages 9-10 of the specification). Figure 3 also references the use of dideoxy nucleotides. Thus, the formation of extension products by Schwartz et al. occurs by using a terminator nucleotide, and not by omitting one of A, T, G, or C as presently claimed.

The primer extension products of the present invention are not full length transcription products of the template polynucleotides. In the present invention, primer extension proceeds down a template until a nucleotide is reached in the template for which no matching nucleotide is present in the nucleotide reaction mixture. In Schwartz et al., primer extension is stopped when a dideoxy nucleotide is incorporated in the transcription product. Accordingly, the process of primer extension disclosed in Schwartz et al. is fundamentally distinguishable from the claimed method. Therefore, Schwartz et al. cannot anticipate claim 41.

**V. REJECTION OF CLAIMS 1-4, 6, 9, 11-15, 18, 20-24, 42, 45 AND 47 UNDER 35 U.S.C. § 103**

Claims 1-4, 6, 9, 11-15, 18, 20-24, 42, 45 and 47 are rejected under 35 U.S.C. § 103 as obvious over Okada et al. in view of Mizusawa et al. (1986) Nucleic Acid Research 14:1319-1324. Applicant respectfully traverses this rejection because the combination of the cited references does not teach or suggest all of the claim elements.

As noted above, Okada et al. fails to teach or suggest a non-terminator nucleotide reaction mixture wherein at least one of A, T, G, or C nucleotides is omitted. Mizusawa et al. fail to cure this deficiency. Mizusawa et al. is cited for teaching non-natural nucleotide analogs. Mizusawa et al. does not teach or suggest forming isometric primer extension products using a non-terminator nucleotide reaction mixture wherein at least one of A, T, G, or C nucleotides is omitted. Accordingly, Applicant submits the rejection should be withdrawn.

**VI. REJECTION OF CLAIMS 19, 25-40, 44, AND 46 UNDER 35 U.S.C. § 103**

Claims 19, 25-40, 44, and 46 are rejected as obvious over Okada et al. in view of Monforte et al. (U.S. Patent 5,965,363) because the combination of references allegedly teaches or suggests all of the claim elements. Applicant respectfully traverses this rejection because neither Okada et al. or Monforte et al., alone or in combination, teach or suggest forming isometric primer extension products using a non-terminator nucleotide reaction mixture wherein at least one of A, T, G, or C nucleotides is omitted.

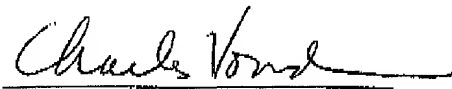
As noted above, Okada et al. fails to teach or suggest a non-terminator nucleotide reaction mixture wherein at least one of A, T, G, or C nucleotides is omitted. Monforte et al. fails to cure this deficiency. Thus, Applicant submits that the combination of Okada et al. with Monforte et al. fails to teach or suggest all of the claim elements and cannot render the claims obvious.

**CONCLUSION**

In light of the foregoing Amendments and Remarks, Applicant believes that the now-pending claims are in condition for allowance. Accordingly, favorable consideration and allowance of the present application is hereby respectfully requested. In the event any fees are due with this paper, please charge these fees to deposit account 20-0778.

Respectfully submitted,

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